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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
CANELLA, KAREN A	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 06/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/897,441	FIBI ET AL.	
	Examiner	Art Unit	
	Karen A Canella	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5-12 and 14-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *9,15 and 16* is/are allowed.

6)☒ Claim(s) *5-7, 10-12, 14, 17-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim 5 has been amended. Claims 5-7, 9-12, and 14-23 are pending and under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

The rejection of claims 10 and 22 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is maintained for reasons of record. Claims 10 and 22 are drawn to methods for purifying EPO, an EPO derivative or an EPO peptide. The claim relies on EPO derivatives. The written description sets forth only EPO peptides on page 3, lines 29-35. The specification mentions but does not teach EPO derivatives, nor does the specification define the genus of EPO derivatives, or provide any examples of EPO derivatives.

The disclosure of a single species may provide an adequate written description of a genus when the species disclosed is representative of the genus. The instant claims encompass full length functional EPO, full length denatured EPO, full length mutant EPO, EPO variants such as truncation mutations, splice variants, allelic variants, which are both functional and non-functional, as well as fragments of EPO which are not fully described. In addition, the instant claims encompass every type of chemical modification which can be carried out on a protein sequence. There is substantial variability among the species of variants encompassed within the scope of the claims because full length normal EPO is only one species descriptive of EPO derivatives. Thus the claims encompasses a genus with widely varying attributes. Furthermore, because the specification has not disclosed or contemplated a specific chemical or protein moiety, the addition of which to full length EPO would constitute an EPO "derivative", full length EPO itself is not representative of a genus of derivatives as no information regarding the chemical structure of an auxiliary moiety attached to EPO has been described.

A description of a genus of molecules may be achieved by means of recitation of a representative number of molecules, defined by structure, falling within the scope of the genus or

a recitation or structural features common to members of the genus, which features constitute a substantial portion of the genus. (Reagents of the University of California v. Eli Lilly, 119 F3d 1559, 1569, 43 USPQ2d 1398-1406, Fed. Cir. 1997).

The written description sets forth the EPO peptides on page 3, lines 29-35, that would be part of some members of the genus, and the art at the time of filing is enabling for full length human EPO and murine EPO. Since the claimed genus encompasses full length EPO proteins beyond human and murine EPO,, in addition to mutants, variants and fragments, etc. attached to undisclosed chemical moieties, the disclosed peptide entities and full length human and murine EPO do not "constitute a substantial portion" of the claimed genus. Therefore, the specification does not provide adequate written description of the claimed genus of EPO derivatives.

Applicant argues that the specification does indeed teach EPO derivatives in Example 7 which illustrates the purification of EPO muteins. This has been considered but not found persuasive. The specification does not define EPO derivatives to encompass only EPO muteins. Further, the text cited by applicant does not disclose the structure of a single EPO mutein but only contemplates EPO muteins as part of the invention. In The Regents of the University of California v. Eli Lilly (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that an 'adequate written description of a DNA...requires a precise definition, such as by structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed chemical invention'. Although this statement was in response to claims drawn to DNA, it is also applicable to claims encompassing a genus of polypeptides. The specification, although contemplating EPO muteins as part of the instant invention, is lacking adequate written description of a single EPO mutein. Further, when given the broadest reasonable interpretation, EPO-derivatives encompass molecules and structures beyond the scope of EPO muteins. Therefore, one of skill in the art would conclude that applicant was not in possession of the genus of EPO derivatives at the time of filing.

Applicant argues that the interpretation of EPO derivatives as broader in scope than EPO muteins contradicts the teachings of the specification. This has been considered but not found persuasive. The examiner is obliged to take the broadest reasonable interpretation. The specification does not provide a definition for "derivative" which would limit the scope to EPO muteins. Applicant argues that even if the specification were not limiting for the term "derivative" the specification contemplates derivatives and thus somehow fulfills the written description requirement by this contemplation. This has been considered but not found persuasive. The muteins contemplated by the specification are not representative of the genus of EPO derivatives for the reasons set forth above.

The rejection of claims 5, 6, 11, 12, 14, 17, 18, 20, 21 and 23 under 35 U.S.C. 102(b) as being anticipated by Lin (US 4,703,008) is maintained for reasons of record.

Claim 6 is drawn in part to an antibody directed against an erythropoietin peptide, wherein said antibody neutralizes the biological activity of EPO and wherein said EPO peptide consists essentially of a peptide of 152 to 166(P2/1). Claim 5 is drawn in part to a method of using erythropoietin peptide consisting essentially of 152 to 166 (P2/1) for the preparation of epitope-specific anti-EPO antibodies, said method comprising immunizing an animal with said peptide and isolating said epitope-specific anti-EPO antibodies. Claim 11 is drawn to a diagnostic aid comprising an antibody of claim 6. Claim 12 is drawn to a diagnostic aid containing and EPO peptide as defined in claim 5. Please note that the recitation of "diagnostic aid" does not constitute a further embodiment of the claimed antibody or peptide and that the recitation of the intended use of said antibody or peptides does not confer patentable distinctness to the products. Claim 23 is drawn to an anti-EPO antibody of claim 6 which is directed to epitopes which bind to the EPO receptor.

Claim 17 is drawn to an anti-erythropoietin antibody directed against epitopes that bind to the EPO receptor. Claim 18 embodies the antibody of claim 17 wherein said antibody neutralizes the biological activity of EPO. Claim 20 is drawn to a "diagnostic" aid containing one or more anti-EPO antibodies of claim 17 for the detection of EPO. Claim 21 is drawn to a "pharmaceutical composition" containing one or more anti-EPO antibodies of claim 17. Please note again that neither "diagnostic aid" nor "pharmaceutical composition" constitutes a claim

limitation, and recitation of the intended use of "detection of EPO" does not impart patentable distinctness to a product.

Lin discloses a method of using erythropoietin peptides consisting of essentially of residues 152-166 for the preparation of epitope-specific anti-EPO antibodies comprising immunization of rabbits with the peptide 144-166 (column 35, lines 21-34). Lin discloses the diagnostic uses of the 144-166 peptide (column 35, line 58 to column 36, line 20). Lin does not specifically disclose that said antibodies were isolated, however, Lin states that the resulting serum antibodies were used to immunoprecipitate 125-I labeled EPO, therefore, it is evident that the antibodies produced by immunization of rabbits with the 144-166 peptide were isolated from the rabbits. Thus Lin anticipates claim 17, and 20 and 21, for the reasons stated above, namely, the recitations of "diagnostic aid" and "pharmaceutical composition" alone do not constitute further embodiments to claims 20 and 21. Lin do not disclose that the antibodies produced from the 144-166 peptide would contain neutralizing antibodies, however, it would be inherent in the anti-144-166 antibodies that a subset of antibodies would be neutralizing as the instant specification is claiming that anti-152-166 antibodies are neutralizing. Therefore, Lin anticipates claim 18, and further claim 6, and the antibodies produced thereby as in claim 5 as well as claims 11 and 23 which have the same scope as claim 6, for the reasons stated above, that claims 11 and 23 do not contain further limitations that would narrow the scope of claim 6. Lin discloses the diagnostic uses for the 144-166 peptide, therefore anticipating claim 12 (column 35, line 58 to column 36, line 20).

Applicant has previously argued that the 144-166 peptide used by Lin does not exhibit biological activity and therefore cannot be an epitope. Applicant states that conclusory statements based on general knowledge or common sense cannot be used to overcome the deficiencies of a reference. However, the examiner was using "common sense" to counter the argument of applicant regarding the lack of biological activity of the isolated peptide. The arguments used by the examiner were not necessary to make the rejection of the instant claims, especially since applicant is arguing limitations that are not part of the claims., such as the requirement of the isolated epitope to possess the same biological activities as the native protein. Lin states that "preliminary in vivo activity studies on the three peptides revealed no significant activity either alone or in combination" has no bearing whatsoever on the antibodies which were raised against these proteins. There is no requirement in the claims for any biological activity attributable to the peptides used to generate the claimed antibodies. Applicants argue that the examiner has not met the high standards of the U.S. Court of Appeals in the allegation that the method of using an erythropoietin peptide for the preparation of epitope-specific anti-EPO

antibodies, an epitope being defined as being composed or one or more peptides, or one or more sections of peptide sequence, wherein said EPO peptide consists essentially of amino acid positions 152 to 166 would inherently comprise the method of using the erythropoietin 144-166 peptide disclosed by Lin. The essential argument seems to be weather of not "consisting essentially of a peptide less than the complete erythropoietin sequence....consisting of 152-166" would be inherently comprised by the 144-166 peptide of Lin. The M.P.E.P (2111.03) states For the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising." See, e.g., PPG, 156 F.3d at 1355, 48 USPQ2d at 1355 ("PPG could have defined the scope of the phrase consisting essentially of' for purposes of its patent by making clear in its specification what it regarded as constituting a material change in the basic and novel characteristics of the invention."). See also In re Janakirama-Rao, 317 F.2d 951, 954, 137 USPQ 893, 895-96 (CCPA 1963). If an applicant contends that additional steps or materials in the prior art are excluded by the recitation of "consisting essentially of," applicant has the burden of showing that the introduction of additional steps or components would materially change the characteristics of applicant's invention. In re De Lajarte, 337 F.2d 870, 143 USPQ 256 (CCPA 1964). See also Ex parte Hoffman, 12 USPQ2d 1061, 1063-64 (Bd. Pat. App. & Inter. 1989) ("Although consisting essentially of' is typically used and defined in the context of compositions of matter, we find nothing intrinsically wrong with the use of such language as a modifier of method steps. . . [rendering] the claim open only for the inclusion of steps which do not materially affect the basic and novel characteristics of the claimed method. To determine the steps included versus excluded the claim must be read in light of the specification. . . . [I]t is an applicant's burden to establish that a step practiced in a prior art method is excluded from his claims by consisting essentially of' language.").

Thus, according to the M.P.E.P., it is applicants burden, not the examiners, to prove that the method of Lin would not anticipate the instant claimed method.

Applicant has previously argues that "the fact that Lin's 144-166 peptide has no in vivo activity support the notion that this peptide does not present the 152-166 epitope properly. Again, this is not persuasive, as limitations regarding the biological activity of the peptide used to raise the antibody are not part of the instant claims. Lin does not specifically disclose that the polyclonal antibodies obtained by immunization with the 144-166 peptide have EPO neutralizing activity. However, it is reasonable to conclude that some of the antibodies which constitute the polyclonal antibodies made by Lin would have the property of reacting with the epitope of EPO consisting of residues 152-166, as these amino acids are included in residues 144-166 and that these antibodies would inherently be neutralizing antibodies, as the specification teaches that the property of binding to residues 152-166 of EPO is commensurate with the property of a neutralizing antibody.

Claim 17 does not specify that the isolated peptide used to simulate an epitope of the full length EPO protein must bind to the EPO receptor in vivo and elicit a biological effect. There are many reasons why a peptide administered in vivo would not elicit the same biological effect

of the parent protein. Firstly, the peptide, out of context of the EPO protein may be rapidly degraded in vivo before binding to the EPO receptor. Secondly, the binding of other epitopes, not included in the peptide used to raise an antibody, may be necessary for increasing the binding affinity of the isolated peptide by altering the steric interaction of residues 144-166 with the EPO receptor, for the reasons given in Philo et al and Narhi et al, supra. The specification teaches that the peptide 152-166 represents an amino acid sequence within EPO which directly binds to the EPO receptor. The peptide used by Lin, 144-166, is the same amino acid sequence with the addition of the eight amino acid sequences which are normally attached to the amino terminus of the 152-166 sequence in the full length EPO protein. As antibodies raised to the 152-166 peptide directly bind the EPO receptor, it is reasonable to conclude that a subset of antibodies raised to the 144-166 peptide also directly binds to the EPO receptor as it contains the 152-166 sequence in addition to adjacent amino acid sequences present in EPO. Further any antibodies which would bind to the residues of 152-166 of EPO would inherently be neutralizing antibodies, as the specification teaches that the property of binding to residues 152-166 of EPO is commensurate with the property of a neutralizing antibody.

Claim 14 is drawn to a pharmaceutical composition containing and antibody directed against an EPO peptide, wherein said peptide neutralizes the biological activity of EPO, and wherein said EPO peptide consists essentially of a peptide of less than the complete EPO protein, said peptide having an amino acid sequence selected from the group consisting of P2 (residues 139-166) and P2/1 (residues 152-166), in accordance with the numbering of the amino acid positions of natural EPO and a pharmaceutically acceptable excipient. The polyclonal antiserum raised to the 144-162 peptide as disclosed by Lin et al would inherently have the characteristics of a pharmaceutical composition as said claimed pharmaceutical composition because the anti-serum of Lin et al would not contain substances which would exclude its use as a pharmaceutical composition.

Applicant has previously argued that the lack of in vivo activity attributed to the 144-166 peptide used by Lin et al to raise polyclonal antibodies teaches against the application of the reference to the instant claims. The examiner has stated above, that the in vivo activity of the peptide is not a claim limitation, and therefore arguments that the Lin peptide does not anticipate the instant invention are moot. Applicant criticizes the examiners explanation for the lack of in vivo activity exhibited by said peptide and adds that the epitope presented by the Lin et al peptide, (144-166) may not present the proper conformation. Applicant does not state what the conformation is in regard to, but the examiner assumes it is in regard to the ability of the peptide to bind to the EPO receptor. This has been considered but not found persuasive. These are claim

limitations which are not part of the instant claim. The issue at hand is whether or not the polyclonal antibodies generated in the host animal in response to the 144-166 peptide would include antibodies which were the same as the instant antibodies claimed. . In order for antibody formation to occur within a host, naïve B-cells of the host must bind to the 144-166 protein. The antibody-protein complex is then taken up by an antigen presenting cell by means of the Fc receptor of the host antibody. The antigen-presenting cell then presents epitopes of the protein in the context of MHC , which thus serves to activate T-cells which can activate B cells which are carrying the complementary receptor. The conformation of the 144-166 peptide will not play a part in the epitopes which are presented by the antigen presenting cell, because a complex protein degradation process takes place within said cell. Further on in the response against said antigen, activated B cells undergo somatic mutation to give antibody producing cells with an even greater heterogeneity. In light of the vast heterogeniety of antibodies which can be produced in a given host, applicant has not provided evidence that antibodies produced in response to the 144-166 peptide will not include antibodies which react with the 152-166 peptide.

Applicant has amended claim 5 to incorporate the limitation "wherein said antibodies neutralize the biological activity of EPO" in order to overcome the rejection of claim 5. This has been considered but not found persuasive. The issue at hand is whether or not the polyclonal antibodies generated in the host animal in response to the 144-166 peptide of Lin et al would include antibodies which were the same as the instant antibodies claimed. The examiner maintains that the polyclonal antiserum generated by Lin et al to the 144-166 peptide would inherently comprise monoclonal antibodies which would be generated by the 152-166 peptide of the instant invention. Applicant has not provided any data to indicate that the neutralizing antibodies generated from the 152-166 peptide were mutually exclusive of the antibodies generated from the 144-166 peptide of Lin et al.

The rejection of claims 5-7, 10-12, 14 and 17-23 under 35 U.S.C. 103(a) as being unpatentable over Miyazaki et al (Journal of immunological Methods, 1988, Vol. 113, pp. 261-267) in view of Lin et al is maintained for reasons of record. The specific embodiments of claims 5, 6, 11, 12, 14, 17, 18, 20, 21 and 23 are taught by Lin et al for the reasons set forth in section 13 above.

Claim 7 is drawn to the antibody of claim 6, wherein said antibody is monoclonal. Claim 10 is drawn to a method of using the antibodies of claim 6 for purifying EPO, EPO derivative or EPO peptide comprising contacting a biological sample with said antibody where said antibody

is bound to a carrier material suitable for chromatography and isolating said EPO, EPO derivative or EPO peptide. Claim 19 is drawn to the antibody of claim 17, wherein said antibody is monoclonal.

Miyazaki et al teach monoclonal antibodies against human erythropoietin, and immunoaffinity columns comprising said monoclonal antibodies and a method of purifying EPO comprising contacting a biological sample with said immunoaffinity column (page 262, under the heading "Materials and methods" and page 263, under the sub-headings "Preparation of an immunoaffinity column" and "Preparation of natural HuEPO"). Miyazaki et al teach the immunoaffinity purification of native EPO by monoclonal antibodies which react with native EPO versus denatured EPO is more desirable than previous methods necessitating the denaturation of EPO before purification page 262, first column, lines (page 267, last two sentences) and more desirable than a previous method using immunoaffinity purification based on monospecific antibodies rather then monoclonal antibodies, wherein said method provided a EPO with reduced biological activity in vivo ((page 261, second column, line 13 to page 262, line 11). Lin et al teaches the specific embodiments of claims 5, 6, 11, 12, 17, 18, 20, 21 and 23 for the reasons set forth above. Lin et al teach that the anti-144-166 antiserum was able to bind human urinary EPO (column 36, lines 27-33). Lin et al suggest but does not teach a methods wherein the 144-166 peptide be used to generate monoclonal antibodies useful in the affinity purification of EPO and EPO-related products (column 35, line 1 to column 36, line 19).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to substitute the 144-166 peptide for the E-rHuEPO and C-rHuEPO used as the immunizing antigen in the method of Miyazaki et al. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Miyazaki et al on the superiority of immunoaffinity columns based on monoclonal antibodies which bind to undenatured EPO.

Applicant has previously argued that since neither of the references teach the limitations of the claims the rejection should be dropped. This rejection is maintained in light of the rejection under 102(b) above

Applicant argues that rejection is inappropriate for reliance upon Lin et al. However, the rejection of the above claims as being anticipated by Lin et al is maintained. Applicant further argues that Miyazaki et al teach away from the instant invention because none of the antibodies neutralized EPO activity. This has been considered but not found persuasive. Miyazaki et al is relied upon for teachings regarding immunoaffinity columns comprising monoclonal antibodies and a method of purifying EPO comprising contacting a biological sample with said

immunoaffinity column. One of skill in the art would known that neutralizing as well as non-neutralizing antibodies can be used in immunoaffinity columns.

The rejection of claims 6, 7, 11, 17-21 for obviousness-type double patenting over claims 1 and 2 of USP 5,712,370 is maintained for reasons of record.

All other rejections and objections as set forth in the previous Office action are withdrawn.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10 a.m. to 9 p.m. M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571)272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Karen A. Canella, Ph.D.
6/7/2004

Karen A. Canella
KAREN A. CANELLA PH.D
PRIMARY EXAMINER